Amendment to the Claims

The claims listed below replace all prior versions and listings of claims in the application.

1. (Currently amended) A method for treating a patient suffering from one or more insulin related ailments selected from the group consisting of hyperglycemia~~, including~~ and hyperglycemia associated with diabetes mellitus, ~~and Alzheimer's disease,~~ which method comprises the step of: administering to a patient in need thereof a therapeutically effective amount of a non-peptidyl compound, which possesses one or more ionic and hydrophobic chemical moieties spatially located so as to mimic the spatial location of at least an ionic or a hydrophobic amino acid residue of insulin and which binds to the insulin binding site of the insulin receptor, wherein said compound is an insulin agonist.

2. (Previously presented) A method according to claim 1, wherein the ionic amino acid residue is selected from the group consisting of: A21 Asn, B21 Glu and A17 Glu.

3. (Original) A method according to claim 1, wherein the ionic and hydrophobic amino acid residue(s) is(are) selected from the group consisting of: A21 Asn, B21 Glu, A17 Glu, B24 Phe, B25 Phe, A19 Tyr, B12 Val, B16 Tyr, A2 Ile, A3 Val and A1 Gly.

4. (Previously presented) A method according to claim 1, wherein at least one amino acid is selected from the group consisting of: A17 Glu, B21 Glu and A21 Asn; and at least one amino acid is selected from the group consisting of: B24 Phe, B25 Phe, A19 Tyr, B12 Val and B16 Tyr.

5. (Previously presented) A method according to claim 1, wherein the non-peptidyl compound possesses ionic and hydrophobic chemical moieties spatially located so as to mimic ionic and hydrophobic residues associated with at least one of the following groups of amino acid residues:

(i.) A21 Asn, B21 Glu, A17 Glu, B24 Phe, B25 Phe;

(ii.) A21 Asn, B21 Glu, B24 Phe, B25 Phe;

(iii.) A21 Asn, B21 Glu, B24 Phe, B25 Phe, A1 Gly, A2 Ile, A3 Val;

(iv.) A21 Asn, B21 Glu, A17 Glu, A19 Tyr, A1 Gly, A2 Ile, A3 Val;

(v.) A21 Asn, B21 Glu, A17 Glu, B12 Val, A1 Gly, A2 Ile, A3 Val;

(vi.) A21 Asn, B21 Glu, B12 Val, A1 Gly, A2 Ile, A3 Val;

(vii.) A21 Asn, B21 Glu, A17 Glu, B16 Tyr, A1 Gly, A2 Ile, A3 Val;

(viii.) A21 Asn, B21 Glu, A17 Glu, A19 Tyr, B12 Val, B16 Tyr;

(ix.) A21 Asn, B21 Glu, A19 Tyr, B12 Val, B16 Tyr;

(x.) A21 Asn, B21 Glu, A17 Glu, B24 Phe, B25 Phe, A19 Tyr, B12 Val, B16 Tyr;

(xi.) A21 Asn, B21 Glu, B24 Phe, B25 Phe, A19 Tyr, B12 Val, B16 Tyr;

(xii) A21 Asn, B21 Glu, B24 Phe, B25 Phe, B12 Val, B16 Tyr;

(xiii.) A21 Asn, B21 Glu, A17 Glu, B24 Phe, B25 Phe, A19 Tyr;

(xiv.) A21 Asn, B21 Glu, B24 Phe, B25 Phe, A19 Tyr;

(xv.) A21 Asn, A17 Glu, B24 Phe, B25 Phe, A19 Tyr;

(xvi.) B21 Glu, A17 Glu, B24 Phe, B25 Phe, A19 Tyr;

(xvii.) A21 Asn, B21 Glu, A17 Glu, B24 Phe, B25 Phe, B12 Val;

(xviii.) A21 Asn, B21 Glu, B24 Phe, B25 Phe, B12 Val;

(xix.) A21 Asn, A17 Glu, B24 Phe, B25 Phe, B12 Val;

(xx.) B21 Glu, A17 Glu, B24 Phe, B25 Phe, B12 Val;

(xxi.) A21 Asn, B21 Glu, A17 Glu, B24 Phe, B25 Phe, B16 Tyr;

(xxii.) A21 Asn, B21 Glu, B24 Phe, B25 Phe, B16 Tyr;

(xxiii.) A21 Asn, A17 Glu, B24 Phe, B25 Phe, B16 Tyr;

(xxiv.) B21 Glu, A17 Glu, B24 Phe, B25 Phe, B16 Tyr;

(xxv.) A21 Asn, B21 Glu, A17 Glu, B24 Phe, A19 Tyr, B12 Val, B16 Tyr;

(xxvi.) A21 Asn, B21 Glu, B24 Phe, A19 Tyr, B12 Val, B16 Tyr;

(xxvii.)A21 Asn, A17 Glu, B24 Phe, A19 Tyr, B12 Val, B16 Tyr;

(xxviii.) B21 Glu, A17 Glu, B24 Phe, A19 Tyr, B12 Val, B16 Tyr;

(xxix.) A21 Asn, B21 Glu, A17 Glu, B25 Phe, A19 Tyr, B12 Val, B16 Tyr;

(xxx.) A21 Asn, B21 Glu, B25 Phe, A19 Tyr, B12 Val, B16 Tyr;

(xxxi.) A21 Asn, A17 Glu, B25 Phe, A19 Tyr, B12 Val, B16 Tyr; and

(xxxii.) B21 Glu, A17 Glu, B25 Phe, A19 Tyr, B12 Val.

6. (Previously presented) A method according to claim 1, wherein the non-peptidyl compound has the following formula:

$AXYXZ_n$ (formula 1)

where A is W or VXW;

V is V_1 or V_2;

V is substituted with up to two X groups;

V_1 is a phenyl or 6 membered heteroaromatic ring, optionally substituted with up to 5 R_1 groups;

V_2 is a 5 member ring system which may incorporate up to 4 hetero atoms which may be independently a nitrogen atom, a nitrogen atom optionally substituted with R_2, oxygen or sulfur, the ring system being optionally substituted with up to 4 R_1 groups;

W is W_1 or W_2 or W_3;

W is substituted with up to two X groups;

W_1 is V_1;

W_2 is a fused bicyclic ring system comprising rings of 5 or 6 atoms, which may incorporate up to 4 hetero atoms, which may be independently a nitrogen atom, a nitrogen atom optionally substituted with R_2, oxygen or sulfur, the system being optionally substituted with up to seven R_1 groups;

W_3 is $-N(R_2)R'_2$;

R_1 is independently H, OH, alkyl, alkenyl, alkynyl, alkoxy, alkanol, hydroxyalkoxy, haloalkyl, haloalkoxy, halogen, SH, thioalkyl, cyano (-CN), $N(R_2)R'_2$, phenyl, phenyl optionally substituted with up to five alkyl groups of 1 to 3 carbon atoms or up to five halogen atoms, benzyl, phenethyl, nitro, $-COR_3$, $-R_5COR_3$, $-R_5SOR_3$, $-R_5SO_2R_3$, $-SO_2N(R_2)R'_2$ or azido;

R_2 and R'_2 are independently H, alkyl of 1 to 6 carbon atoms, alkenyl of 3 to 6 carbon atoms, alkynyl of 3 to 6 carbons, hydroxyalkyl of 2 to 6 carbons, alkoxy of 2 to 6 carbons, haloalkyl, haloalkenyl, haloalkoxy, benzyl, benzyl optionally substituted with up to four R_1 groups, phenylethyl, phenylethyl optionally

substituted with up to four R_1 groups, arylalkyl, and where R_2 and R'_2 can also be joined to form cyclic structures;

R_3 is independently H, OH, alkyl, alkenyl, alkynyl, alkoxy, alkanol, hydroxyalkoxy, $-R_4N(R_2)R'_2$, mesyl, triflouromesyl, $-NHSO_2CH_3$ or $-NHSO_2CF_3$;

R_4 is independently a bond, alkyl, alkenyl or alkynyl;

X is independently, a bond, $-R_4N(R_2)R_4-$, $-R_4N{=}NR_4-$, $-R_4N(R_2)-N(R_2)R_4-$, $-R_4OR_4-$, $-R_4SR_4-$, $-R_5-$, $-R_5O-$, $-R_5S-$, $-R_5N(R_2)-$, -SO-, sulfonyl ($-SO_2-$), -CO-, -CONH-, -NHCONH-, -NHCO-, -CONHCO-, $-CON(R_2)-$, $-R_5COR_5-$, $-R_5COR_5N(R_2)R_5-$, $-N(R_2)CO-$ or $-R_4N(R_2)R_4COR_4-$;

R_5 is independently alkyl, alkenyl, alkynyl, alkoxy, alkanol, hydroxyalkoxy;

Y is either Y_1, Y_2 or Y_3;

Y is substituted with at least two, but optionally up to four X linking groups;

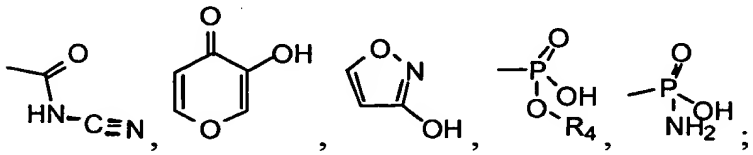
Y_1 is a fused bicyclic ring system comprising rings of 5 or 6 atoms which may incorporate up to 4 hetero atoms, which may be independently a nitrogen atom, a nitrogen atom optionally substituted with R_2, oxygen or sulfur, the ring system optionally independently incorporating a sulfoxide (SO), sulfone (SO_2) or carbonyl (CO) group and optionally up to seven R_1 groups;

Y_2 is a 6:6:6 or a 6:5:6 fused tricyclic system which may incorporate up to 4 hetero atoms which may be independently a nitrogen atom, a nitrogen atom optionally substituted with R_2, oxygen or sulfur, the ring system optionally independently incorporating a sulfoxide (SO), sulfone (SO_2) or carbonyl (CO) group, and the ring system being substituted with at least two, but optionally up to four X linking groups and optionally up to seven R_1 groups;

Y_3 is V_1;

Z is independently $-R_6COOH$, $-R_6SO_3H$, $-R_6NO_2$, $-R_6SO_2H$, $-R_6SO_2NHR_2$; $-R_7SO_2NHCOR_4$ -N-trifluoromesylsulfonamidate, -OH, -2-yl-hydroxyethanoic acid (-CH(OH)COOH), -3-yl-2-hydroxypropanoic acid ($-CH_2CH(OH)COOH$) -2-yl-2-hydroxypropanoic acid ($-CH(CH_3)(OH)COOH$), -3-yl-2,3-dihydroxypropanoic acid (-CH(OH)CH(OH)COOH), -2-yl-2,3-dihydroxypropanoic acid ($-C(CH_2(OH))(OH)COOH$), -3-yl-2-hydroxypropan-3-one-1-oic acid (-COCH(OH)COOH, 2-yl-2-hydroxypropandioic acid (-C(COOH)(OH)COOH), -2-

yl-propandioic acid (-C(COOH)(H)COOH), -4-yl-2-hydroxybutan-4-one-1-oic acid (-$COCH_2CH(OH)COOH$, 2-yl-2-hydroxybutan-1,4-dioic acid (-$C(OH)(COOH)CH_2COOH$), 3-yl-2-hydroxybutan-1,4-dioic acid (-CH(CH(OH)COOH)COOH), 5-yl-tetrazole,



R_6 is independently a bond, alkyl, alkenyl, alkynyl, alkoxy, $-CO(CH_2)_n-$, where n is an integer between 0 and 4, alkanoic, alkenoic or alkynoic;
with the exception that where W_1 is an optionally substituted phenyl then Y_3 cannot be an optionally substituted phenyl.

7. (Original) A method according to claim 6, wherein the non-peptidyl compound is a dimer or heterodimer wherein the compounds are joined through a X linking group by way of their V or W groups.

8. (Previously presented) A method according to claim 6, wherein when V is V_1 or V_2, then:

V_1 is selected from the group consisting of, benzene, pyridine, pyridazine, pyrimidine, pyrazine and triazine and is optionally substituted with up to 5 R_1 groups; and

V_2 is selected from the group consisting of, cyclopenta-1,3-diene, pyrrole, furan, thiophene, oxazole, isoxazole, pyrazole, imidazole, thiazole, isothiazole and triazole and is optionally substituted with up to 4 R_1 groups;

and W is W_2 then

W_2 is selected from the group consisting of naphthalene, quinoline, isoquinoline, phthalazine, naphthyridine, quinoxaline, quinazoline, cinnoline, pteridine, indole, benzothiophene, benzofuran, benzimidazole, indazole, benzoxazole, benzisooxazole, benzthiazole, benzisothiazole, purine, indoline and isoindoline and is optionally substituted with up to seven R_1 groups;

and Y is either Y_1 or Y_2 then

Y_1 is selected from the group consisting of croman, isochroman, benzofuran, cromene, 1,2,3,4-tetrahydronaphthalene, 1,4-dihydronaphthalene, indan, indene, benzopiperidine, indoline, isoindoline, quinoline, isoquinoline, phthalazine, naphthyridine, quinoxaline, quinazoline, cinnoline or pteridine, coumarin and 2,3-dihydrocoumarin and is optionally substituted with up to seven R_1 groups; and Y_2 is selected from the group consisting of 9H-xanthone, 9H-xanthene, phenoxathiin, phenoxathiin-10-oxide, phenoxathiin-10-dioxide, acridine, phenazine, phenothiazine, phenoxazine, phenothiazine-5-oxide, phenothiazine-5-dioxide, thiathrene-5-dioxide, thiathrene-5-oxide, carbazole, dibenzo[b,d]furan and dibenzo[b,d]thiophene and is optionally substituted with up to seven R_1 groups.

9. (Original) A method according to claim 6, wherein when A is VXW then:V is phenyl or pyrazole, optionally substituted with up to 5 R_1 groups;and when A is W or VXW then W is W_1, W_2 or W_3 wherein W_1 is phenyl optionally substituted with up to 5 R_1 groups;

W_2 is naphthalene or quinoline optionally substituted with up to seven R_1 groups wherein R_1 is independently H, OH, methyl, ethyl, propyl, nitro, methoxy, ethoxy, 2-hydroxyethoxy, chloro, fluoro or acetyl;

W_3 is $-N(R_2)R_2$ wherein R_2 is propyl; X is independently, a bond, methoxy ($-OCH_2$), oxypropoxy ($-O(CH_2)_3O-$), hexenyloxy ($-O(CH_2)_4CH=CH-$), sulfonyloxy ($-SO_2O-$), methyl ($-CH_2-$), amidyl (-CONH-) or -NHCONH-; and Y is either Y_1 or Y_2 then Y_1 is croman, 4-H-chromen-4-one or napthalene optionally substituted with up to seven R_1 groups wherein R_1 is independently H, OH, methyl, ethyl, propyl, nitro, methoxy, ethoxy, 2-hydroxyethoxy, chloro, fluoro or acetyl;

Y_2 is 9H-xanthone optionally substituted with up to seven R_1 groups wherein R_1 is independently H, OH, methyl, ethyl, propyl, nitro, methoxy, ethoxy, 2-hydroxyethoxy, chloro, fluoro or acetyl;

Y_3 is phenyl optionally substituted with up to 5 R_1 groups wherein R_1 is independently H, OH, methyl, ethyl, propyl, nitro, methoxy, ethoxy, 2-hydroxyethoxy, chloro, fluoro or acetyl; and

Z is independently $-R_6COOH$, $-R_6SO_3H$ or -N-trifluoromesylsulfonamidate wherein R_6 is independently a bond or propyl.

10. (Previously presented) A method according to claim 6, wherein the non-peptidyl compound is selected from the following group of compounds:

(i.) 4,4'-Methylenebis[3-hydroxy-2-naphthalenecarboxylic acid];

(ii.) 7-[3-(4-acetyl-2-ethyl-5-hydroxyphenoxy)propoxy]-3,4-dihydro-8-propyl-2H-1-benzopyran-2-carboxylic acid;

(iii.) 2,4-dichloro-6-(*N*-(trifluoromethanesulfonyl))sulfamoylphenyl 3,5-dichloro-2-hydroxybenzenesulfonate;

(iv.) 7-[(4-acetyl-3-hydroxy-2-propylphenyl)methoxy]-4-oxo-8-propyl-4*H*-1-benzopyran-2-carboxylic acid;

(v.) 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl-2*H*-1-benzopyran-2-carboxylic acid;

(vi.) 3,4-dihydro-8-propyl-7-[[3-[2-ethyl-5-hydroxy-4-(1*H*-pyrazol-3-yl)phenoxy]propyl]oxy]-2*H*-1-benzopyran-2-carboxylic acid;

(vii.) 3,4-dihydro-8-propyl-7-[[3-[2-ethyl-5-hydroxy-4-ethoxyphenoxy]propyl]oxy]-2*H*-1-benzopyran-2-carboxylic acid;

(viii.) 3-[4-[7-carboxy-9-oxo-3-[3-[2-ethyl-4-(4-fluorophenyl)-5-hydroxyphenoxy]propoxy]-9*H*-xanthene]]propanoic acid; ~~or~~

(ix.) 8-propyl-7-(quinol-2'-ylmethoxy)-3,4-dihydro-2*H*-1-benzopyran-2-carboxylic acid;

(x.) 7-(naphth-2'-ylmethoxy)-8-propyl-3,4-dihydro-2*H*-1-benzopyran-2-carboxylic acid; (xi.) *N*-(trifluoromethanesulfonyl)-3,5-dinitro-4-(*N'*,*N'*-dipropylamino)benzenesulfonamide;

(xii.) 8-propyl-7-[3-[4-(4-fluorophenyl)-2-ethyl-5-hydroxyphenoxy]propoxy]-3,4-dihydro-2H-1-benzopyran-2-carboxylic acid;

(xiii.) 3,4-dihydro-7-[[6-(4-methoxyphenyl)hexenyl]oxy]-8-propyl-2H-1-benzopyran-2-carboxylic acid; ~~or~~ and

(xiv.) 8,8'-[Carbonylbis[imino-3,1-phenylenecarbonylimino(4-methyl-3,1-phenylene)carbonylimino]]bis-1,3,5-naphthalenetrisulfonic acid.

11-15. (Canceled)

16. (Currently amended) A method for identifying a non-peptidyl compound possessing ionic and hydrophobic chemical moieties spatially located so as to mimic particular ionic and hydrophobic amino acid residues of insulin and which binds to the insulin binding site of the insulin receptor, said method comprising the steps of: (1) comparing the three dimensional structure of the non-peptidyl compound with a three dimensional pharmacophore of an active site of insulin; and (2) selecting a non-peptidyl compound with ionic and hydrophobic chemical moieties spatially located so as to mimic said site.

17. (Original) A method for determining whether a non-peptidyl compound identified according to the method of claim 16 is an agonist or an antagonist, said method comprising the step of: exposing the compound to an insulin or insulin like receptor and measuring the change in biological activity following exposure of the compound to the receptor.

18-19. (Canceled)

20. (Previously presented) A method according to claim 6 wherein V_1 is selected from the group consisting of: benzene, pyridine, pyridazine, pyrimidine, pyrazine and triazine.

21. (Previously presented) A method according to claim 6 wherein V_2 is selected from the group consisting of: cyclopenta-1,3-diene, pyrrole, furan, thiophene, oxazole, isoxazole, pyrazole, imidazole, thiazole, isothiazole and triazole, optionally substituted with up to 4 R_1 groups.

22. (Previously presented) A method according to claim 6 wherein W_2 is selected from the group consisting of: naphthalene, quinoline, isoquinoline, phthalazine,

naphthyridine, quinoxaline, quinazoline, cinnoline, pteridine, indole, benzothiophene, benzofuran, benzimidazole, indazole, benzoxazole, benzisooxazole, benzthiazole, benzisothiazole, purine, indoline and isoindoline.

23. (Previously presented) A method according to claim 6 wherein R_2 and R'_2 are joined to form cyclic structures selected from the group consisting of : pyrrolidine, piperidine, hexahydro-1H-azepine, morpholine and piperazine.

24. (Previously presented) A method according to claim 6 wherein Y_1 is selected from the group consisting of: croman, isochroman, benzofuran, cromene, 1,2,3,4-tetrahydronaphthalene, 1,4-dihydronaphthalene, indan, indene, benzopiperidine, indoline, isoindoline, quinoline, isoquinoline, phthalazine, naphthyridine, quinoxaline, quinazoline, cinnoline pteridine, coumarin and 2,3-dihydrocoumarin.

25. (Previously presented) A method according to claim 6 wherein Y_2 is selected from the group consisting of: 9H-xanthone, 9H-xanthene, phenoxathiin, phenoxathiin-10-oxide, phenoxathiin-10-dioxide, acridine, phenazine, phenothiazine, phenoxazine, phenothiazine-5-oxide, phenothiazine-5-dioxide, thiathrene-5-dioxide, thiathrene-5-oxide, carbazole, dibenzo[b,d]furan and dibenzo[b,d]thiophene.

26-31. (Canceled)

32. (Currently amended) A method for treating a patient suffering from one or more insulin related ailments selected from the group consisting of hypoglycemia, insulinomas, insulin and hypoglycemic drug overdose, gastric dumping syndrome and congenital hyperinsulinism, which method comprises the step of: administering to a patient in need thereof a therapeutically effective amount of a non-peptidyl compound which possesses one or more ionic and hydrophobic chemical moieties spatially located so as to mimic the spatial location of at least an ionic or a hydrophobic amino acid residue of insulin and which binds to the insulin binding site of the insulin receptor, wherein said compound is an insulin antagonist.

33. (Previously presented) A method according to claim 32, wherein the ionic amino acid residue is selected from the group consisting of: A21 Asn, B21 Glu and A17 Glu.

34. (Previously presented) A method according to claim 32, wherein the ionic and hydrophobic amino acid residue(s) is(are) selected from the group consisting of: A21 Asn,

B21 Glu, A17 Glu, B24 Phe, B25 Phe, A19 Tyr, B12 Val, B16 Tyr, A2 Ile, A3 Val and A1 Gly.

35. (Previously presented) A method according to claim 32, wherein at least one amino acid is selected from the group consisting of: A17 Glu, B21 Glu and A21 Asn; and at least one amino acid is selected from the group consisting of: B24 Phe, B25 Phe, A19 Tyr, B12 Val and B16 Tyr.

36. (Previously presented) A method according to claim 32, wherein the non-peptidyl compound possesses ionic and hydrophobic chemical moieties spatially located so as to mimic ionic and hydrophobic residues associated with at least one of the following groups of amino acid residues:

(i.) A21 Asn, B21 Glu, A17 Glu, B24 Phe, B25 Phe;

(ii.) A21 Asn, B21 Glu, B24 Phe, B25 Phe;

(iii.) A21 Asn, B21 Glu, B24 Phe, B25 Phe, A1 Gly, A2 Ile, A3 Val;

(iv.) A21 Asn, B21 Glu, A17 Glu, A19 Tyr, A1 Gly, A2 Ile, A3 Val;

(v.) A21 Asn, B21 Glu, A17 Glu, B12 Val, A1 Gly, A2 Ile, A3 Val;

(vi.) A21 Asn, B21 Glu, B12 Val, A1 Gly, A2 Ile, A3 Val;

(vii.) A21 Asn, B21 Glu, A17 Glu, B16 Tyr, A1 Gly, A2 Ile, A3 Val;

(viii) A21 Asn, B21 Glu, A17 Glu, A19 Tyr, B12 Val, B16 Tyr;

(ix.) A21 Asn, B21 Glu, A19 Tyr, B12 Val, B16 Tyr;

(x.) A21 Asn, B21 Glu, A17 Glu, B24 Phe, B25 Phe, A19 Tyr, B12 Val, B16 Tyr;

(xi.) A21 Asn, B21 Glu, B24 Phe, B25 Phe, A19 Tyr, B12 Val, B16 Tyr;

(xii) A21 Asn, B21 Glu, B24 Phe, B25 Phe, B12 Val, B16 Tyr;

(xiii.) A21 Asn, B21 Glu, A17 Glu, B24 Phe, B25 Phe, A19 Tyr;

(xiv.) A21 Asn, B21 Glu, B24 Phe, B25 Phe, A19 Tyr;

(xv.) A21 Asn, A17 Glu, B24 Phe, B25 Phe, A19 Tyr;

(xvi.) B21 Glu, A17 Glu, B24 Phe, B25 Phe, A19 Tyr;

(xvii.) A21 Asn, B21 Glu, A17 Glu, B24 Phe, B25 Phe, B12 Val;

(xviii.) A21 Asn, B21 Glu, B24 Phe, B25 Phe, B12 Val;

(xix.) A21 Asn, A17 Glu, B24 Phe, B25 Phe, B12 Val;

(xx.) B21 Glu, A17 Glu, B24 Phe, B25 Phe, B12 Val;

(xxi.) A21 Asn, B21 Glu, A17 Glu, B24 Phe, B25 Phe, B16 Tyr;

(xxii.) A21 Asn, B21 Glu, B24 Phe, B25 Phe, B16 Tyr;

(xxiii.) A21 Asn, A17 Glu, B24 Phe, B25 Phe, B16 Tyr;

(xxiv.) B21 Glu, A17 Glu, B24 Phe, B25 Phe, B16 Tyr;

(xxv.) A21 Asn, B21 Glu, A17 Glu, B24 Phe, A19 Tyr, B12 Val, B16 Tyr;

(xxvi.) A21 Asn, B21 Glu, B24 Phe, A19 Tyr, B12 Val, B16 Tyr;

(xxvii.)A21 Asn, A17 Glu, B24 Phe, A19 Tyr, B12 Val, B16 Tyr;

(xxviii.) B21 Glu, A17 Glu, B24 Phe, A19 Tyr, B12 Val, B16 Tyr;

(xxix.) A21 Asn, B21 Glu, A17 Glu, B25 Phe, A19 Tyr, B12 Val, B16 Tyr;

(xxx.) A21 Asn, B21 Glu, B25 Phe, A19 Tyr, B12 Val, B16 Tyr;

(xxxi.) A21 Asn, A17 Glu, B25 Phe, A19 Tyr, B12 Val, B16 Tyr; and

(xxxii.) B21 Glu, A17 Glu, B25 Phe, A19 Tyr, B12 Val.

37. (Previously presented) A method according to claim 32, wherein the non-peptidyl compound has the following formula:

$AXYXZ_n$ (formula 1)

where A is W or VXW;

V is V_1 or V_2;

V is substituted with up to two X groups;

V_1 is a phenyl or 6 membered heteroaromatic ring, optionally substituted with up to 5 R_1 groups;

V_2 is a 5 member ring system which may incorporate up to 4 hetero atoms which may be independently a nitrogen atom, a nitrogen atom optionally substituted with R_2, oxygen or sulfur, the ring system being optionally substituted with up to 4 R_1 groups;

W is W_1 or W_2 or W_3;

W is substituted with up to two X groups;

W_1 is V_1;

W_2 is a fused bicyclic ring system comprising rings of 5 or 6 atoms, which may incorporate up to 4 hetero atoms, which may be independently a nitrogen atom, a nitrogen atom optionally substituted with R_2, oxygen or sulfur, the system being optionally substituted with up to seven R_1 groups;

W_3 is $-N(R_2)R'_2$;

R_1 is independently H, OH, alkyl, alkenyl, alkynyl, alkoxy, alkanol, hydroxyalkoxy, haloalkyl, haloalkoxy, halogen, SH, thioalkyl, cyano (-CN), $N(R_2)R'_2$, phenyl, phenyl optionally substituted with up to five alkyl groups of 1 to 3 carbon atoms or up to five halogen atoms, benzyl, phenethyl, nitro, $-COR_3$, $-R_5COR_3$, $-R_5SOR_3$, $-R_5SO_2R_3$, $-SO_2N(R_2)R'_2$ or azido;

R_2 and R'_2 are independently H, alkyl of 1 to 6 carbon atoms, alkenyl of 3 to 6 carbon atoms, alkynyl of 3 to 6 carbons, hydroxyalkyl of 2 to 6 carbons, alkoxy of 2 to 6 carbons, haloalkyl, haloalkenyl, haloalkoxy, benzyl, benzyl optionally substituted with up to four R_1 groups, phenylethyl, phenylethyl optionally substituted with up to four R_1 groups, arylalkyl, and where R_2 and R'_2 can also be joined to form cyclic structures;

R_3 is independently H, OH, alkyl, alkenyl, alkynyl, alkoxy, alkanol, hydroxyalkoxy, $-R_4N(R_2)R'_2$, mesyl, triflouromesyl, $-NHSO_2CH_3$ or $-NHSO_2CF_3$;

R_4 is independently a bond, alkyl, alkenyl or alkynyl;

X is independently, a bond, $-R_4N(R_2)R_4-$, $-R_4N{=}NR_4-$, $-R_4N(R_2)-N(R_2)R_4-$, $-R_4OR_4$, $-R_4SR_4-$, $-R_5-$, $-R_5O-$, $-R_5S-$, $-R_5N(R_2)-$, -SO-, sulfonyl ($-SO_2-$), -CO-, -CONH-, -NHCONH-, -NHCO-, -CONHCO-, $-CON(R_2)-$, $-R_5COR_5-$, $-R_5COR_5N(R_2)R_5-$, $-N(R_2)CO-$ or $-R_4N(R_2)R_4COR_4-$;

R_5 is independently alkyl, alkenyl, alkynyl, alkoxy, alkanol, hydroxyalkoxy;

Y is either Y_1, Y_2 or Y_3;

Y is substituted with at least two, but optionally up to four X linking groups;

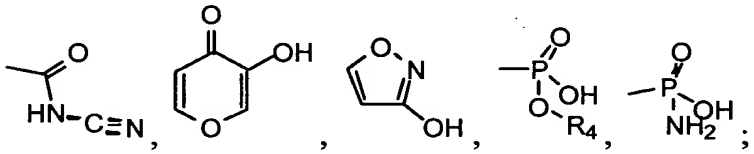
Y_1 is a fused bicyclic ring system comprising rings of 5 or 6 atoms which may incorporate up to 4 hetero atoms, which may be independently a nitrogen atom, a

nitrogen atom optionally substituted with R_2, oxygen or sulfur, the ring system optionally independently incorporating a sulfoxide (SO), sulfone (SO_2) or carbonyl (CO) group and optionally up to seven R_1 groups;

Y_2 is a 6:6:6 or a 6:5:6 fused tricyclic system which may incorporate up to 4 hetero atoms which may be independently a nitrogen atom, a nitrogen atom optionally substituted with R_2, oxygen or sulfur, the ring system optionally independently incorporating a sulfoxide (SO), sulfone (SO_2) or carbonyl (CO) group, and the ring system being substituted with at least two, but optionally up to four X linking groups and optionally up to seven R_1 groups;

Y_3 is V_1;

Z is independently $-R_6COOH$, $-R_6SO_3H$, $-R_6NO_2$, $-R_6SO_2H$, $-R_6SO_2NHR_2$; $-R_7SO_2NHCOR_4$ -N-trifluoromesylsulfonamidate, -OH, -2-yl-hydroxyethanoic acid (-CH(OH)COOH), -3-yl-2-hydroxypropanoic acid ($-CH_2CH(OH)COOH$) -2-yl-2-hydroxypropanoic acid ($-CH(CH_3)(OH)COOH$), -3-yl-2,3-dihydroxypropanoic acid (-CH(OH)CH(OH)COOH), -2-yl-2,3-dihydroxypropanoic acid ($-C(CH_2(OH))(OH)COOH$), -3-yl-2-hydroxypropan-3-one-1-oic acid (-COCH(OH)COOH, 2-yl-2-hydroxypropandioic acid (-C(COOH)(OH)COOH), -2-yl-propandioic acid (-C(COOH)(H)COOH), -4-yl-2-hydroxybutan-4-one-1-oic acid ($-COCH_2CH(OH)COOH$, 2-yl-2-hydroxybutan-1,4-dioic acid ($-C(OH)(COOH)CH_2COOH$), 3-yl-2-hydroxybutan-1,4-dioic acid (-CH(CH(OH)COOH)COOH), 5-yl-tetrazole,



R_6 is independently a bond, alkyl, alkenyl, alkynyl, alkoxy, $-CO(CH_2)_n-$, where n is an integer between 0 and 4, alkanoic, alkenoic or alkynoic;

with the exception that where W_1 is an optionally substituted phenyl then Y_3 cannot be an optionally substituted phenyl.

38. (Previously presented) A method according to claim 37, wherein the non-peptidyl compound is a dimer or heterodimer wherein the compounds are joined through a X linking group by way of their V or W groups.

39. (Previously presented) A method according to claim 37, wherein when V is V_1 or V_2, then:

V_1 is selected from the group consisting of, benzene, pyridine, pyridazine, pyrimidine, pyrazine and triazine and is optionally substituted with up to 5 R_1 groups; and

V_2 is selected from the group consisting of, cyclopenta-1,3-diene, pyrrole, furan, thiophene, oxazole, isoxazole, pyrazole, imidazole, thiazole, isothiazole and triazole and is optionally substituted with up to 4 R_1 groups;

and W is W_2 then

W_2 is selected from the group consisting of naphthalene, quinoline, isoquinoline, phthalazine, naphthyridine, quinoxaline, quinazoline, cinnoline, pteridine, indole, benzothiophene, benzofuran, benzimidazole, indazole, benzoxazole, benzisooxazole, benzthiazole, benzisothiazole, purine, indoline and isoindoline and is optionally substituted with up to seven R_1 groups; and Y is either Y_1 or Y_2 then

Y_1 is selected from the group consisting of croman, isochroman, benzofuran, cromene, 1,2,3,4-tetrahydronaphthalene, 1,4-dihydronaphthalene, indan, indene, benzopiperidine, indoline, isoindoline, quinoline, isoquinoline, phthalazine, naphthyridine, quinoxaline, quinazoline, cinnoline or pteridine, coumarin and 2,3-dihydrocoumarin and is optionally substituted with up to seven R_1 groups; and

Y_2 is selected from the group consisting of 9H-xanthone, 9H-xanthene, phenoxathiin, phenoxathiin-10-oxide, phenoxathiin-10-dioxide, acridine, phenazine, phenothiazine, phenoxazine, phenothiazine-5-oxide, phenothiazine-5-dioxide, thiathrene-5-dioxide, thiathrene-5-oxide, carbazole, dibenzo[b,d]furan and dibenzo[b,d]thiophene and is optionally substituted with up to seven R_1 groups.

40. (Previously presented) A method according to claim 37, wherein when A is VXW then:

V is phenyl or pyrazole, optionally substituted with up to 5 R_1 groups;

and when A is W or VXW then W is W_1, W_2 or W_3 wherein

W_1 is phenyl optionally substituted with up to 5 R_1 groups;

W_2 is naphthalene or quinoline optionally substituted with up to seven R_1 groups wherein R_1 is independently H, OH, methyl, ethyl, propyl, nitro, methoxy, ethoxy, 2-hydroxyethoxy, chloro, fluoro or acetyl;

W_3 is $-N(R_2)R_2$ wherein R_2 is propyl;

X is independently, a bond, methoxy ($-OCH_2-$), oxypropoxy ($-O(CH_2)_3O-$), hexenyloxy ($-O(CH_2)_4CH=CH-$), sulfonyloxy ($-SO_2O-$), methyl ($-CH_2-$), amidyl (-CONH-) or -NHCONH-; and Y is either Y_1 or Y_2 then

Y_1 is croman, 4-H-chromen-4-one or napthalene optionally substituted with up to seven R_1 groups wherein R_1 is independently H, OH, methyl, ethyl, propyl, nitro, methoxy, ethoxy, 2-hydroxyethoxy, chloro, fluoro or acetyl;

Y_2 is 9H-xanthone optionally substituted with up to seven R_1 groups wherein R_1 is independently H, OH, methyl, ethyl, propyl, nitro, methoxy, ethoxy, 2-hydroxyethoxy, chloro, fluoro or acetyl;

Y_3 is phenyl optionally substituted with up to 5 R_1 groups wherein R_1 is independently H, OH, methyl, ethyl, propyl, nitro, methoxy, ethoxy, 2-hydroxyethoxy, chloro, fluoro or acetyl; and

Z is independently $-R_6COOH$, $-R_6SO_3H$ or -N-trifluoromesylsulfonamidate wherein R_6 is independently a bond or propyl.

41. (Previously presented) A method according to claim 37, wherein the non-peptidyl compound is selected from the following group of compounds:

(i.) 4,4'-Methylenebis[3-hydroxy-2-naphthalenecarboxylic acid];

(ii.) 7-[3-(4-acetyl-2-ethyl-5-hydroxyphenoxy)propoxy]-3,4-dihydro-8-propyl-2H-1-benzopyran-2-carboxylic acid;

(iii.) 2,4-dichloro-6-(*N*-(trifluoromethanesulfonyl))sulfamoylphenyl 3,5-dichloro-2-hydroxybenzenesulfonate;

(iv.) 7-[(4-acetyl-3-hydroxy-2-propylphenyl)methoxy]-4-oxo-8-propyl-4*H*-1-benzopyran-2-carboxylic acid;

(v.) 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl-2*H*-1-benzopyran-2-carboxylic acid;

(vi.) 3,4-dihydro-8-propyl-7-[[3-[2-ethyl-5-hydroxy-4-(1*H*-pyrazol-3-yl)phenoxy]propyl]oxy]-2*H*-1-benzopyran-2-carboxylic acid;

(vii.) 3,4-dihydro-8-propyl-7-[[3-[2-ethyl-5-hydroxy-4-ethoxyphenoxy]propyl]oxy]-2*H*-1-benzopyran-2-carboxylic acid;

(viii.) 3-[4-[7-carboxy-9-oxo-3-[3-[2-ethyl-4-(4-fluorophenyl)-5-hydroxyphenoxy]propoxy]-9*H*-xanthene]]propanoic acid;

(ix.) 8-propyl-7-(quinol-2'-ylmethoxy)-3,4-dihydro-2*H*-1-benzopyran-2-carboxylic acid;

(x.) 7-(naphth-2'-ylmethoxy)-8-propyl-3,4-dihydro-2*H*-1-benzopyran-2-carboxylic acid;

(xi.) *N*-(trifluoromethanesulfonyl)-3,5-dinitro-4-(*N*',*N*'-dipropylamino)benzenesulfonamide;

(xii.) 8-propyl-7-[3-[4-(4-fluorophenyl)-2-ethyl-5-hydroxyphenoxy]propoxy]-3,4-dihydro-2H-1-benzopyran-2-carboxylic acid; and

(xiii.) 3,4-dihydro-7-[[6-(4-methoxyphenyl)hexenyl]oxy]-8-propyl-2H-1-benzopyran-2-carboxylic acid;

42. (Previously presented) A method according to claim 37 wherein V_1 is selected from the group consisting of: benzene, pyridine, pyridazine, pyrimidine, pyrazine and triazine.

43. (Previously presented) A method according to claim 37 wherein V_2 is selected from the group consisting of: cyclopenta-1,3-diene, pyrrole, furan, thiophene, oxazole, isoxazole, pyrazole, imidazole, thiazole, isothiazole and triazole, optionally substituted with up to 4 R_1 groups.

44. (Previously presented) A method according to claim 37 wherein W_2 is selected from the group consisting of: naphthalene, quinoline, isoquinoline, phthalazine, naphthyridine, quinoxaline, quinazoline, cinnoline, pteridine, indole, benzothiophene, benzofuran, benzimidazole, indazole, benzoxazole, benzisooxazole, benzthiazole, benzisothiazole, purine, indoline and isoindoline.

45. (Previously presented) A method according to claim 37 wherein R_2 and R'_2 are joined to form cyclic structures selected from the group consisting of : pyrrolidine, piperidine, hexahydro-1H-azepine, morpholine and piperazine.

46. (Previously presented) A method according to claim 37 wherein Y_1 is selected from the group consisting of: croman, isochroman, benzofuran, cromene, 1,2,3,4-tetrahydronaphthalene, 1,4-dihydronaphthalene, indan, indene, benzopiperidine, indoline, isoindoline, quinoline, isoquinoline, phthalazine, naphthyridine, quinoxaline, quinazoline, cinnoline or pteridine, coumarin and 2,3-dihydrocoumarin.

47. (Previously presented) A method according to claim 37 wherein Y_2 is selected from the group consisting of: 9H-xanthone, 9H-xanthene, phenoxathiin, phenoxathiin-10-oxide, phenoxathiin-10-dioxide, acridine, phenazine, phenothiazine, phenoxazine, phenothiazine-5-oxide, phenothiazine-5-dioxide, thiathrene-5-dioxide, thiathrene-5-oxide, carbazole, dibenzo[b,d]furan and dibenzo[b,d]thiophene